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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/950,082	09/12/2001	Craig A. Rosen	PS-804	9299

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HUMAN GENOME SCIENCES INC
9410 KEY WEST AVENUE
ROCKVILLE, MD 20850

EXAMINER
SHEINBERG, MONIKA B

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/950,082	ROSEN ET AL.	
	Examin r	Art Unit	
	Monika B Sheinberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8,13,15,17-20,22 and 24-57* is/are pending in the application.

4a) Of the above claim(s) *1,8,13,15,17-20 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-57* is/are rejected.

7)☒ Claim(s) *50-57* is/are objected to.

8)☒ Claim(s) *1,8,13,15,17-20,22 and 24-57* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to the Preliminary Amendment and Election filed: 25 March 2003

Election/Restrictions

Applicant's election with traverse of Group III (claims 11, 12 and 16) and polypeptide sequence election of SEQ ID NO: 764; in the response filed: 25 March 2003, is acknowledged. The traversal is on the ground(s) that it would not be a serious search burden on the Examiner since "the searches for polynucleotides, polypeptides, antibodies, and methods of diagnosing and treating disease states using the proteins of the subject invention would clearly be overlapping" (p.11, 4th paragraph). This is not found persuasive because the inventions are distinct for the reasons given in the previous Office action; they have acquired a separate status in the art because of their recognized divergent subject matter. The completely separate chemical types of the inventions of the nucleic acid, polypeptide, and antibody Groups supports the undue search burden if all were examined together.

The requirement is still deemed proper and is therefore made FINAL.

- The cancellation of claims 2-7, 9-12, 14, 16, 21 and 23; the amendments made to claims 1, 8, 13, 15, 17-20 and 22; and the addition of new claims 24-57, are acknowledged.
- Claims 1, 8, 13, 15, 17-20, 22 and 24-57 are pending.
- Claims 1, 8, 13, 15, 17-20 and 22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the response filed: 25 March 2003.
- Claims 24-57, drawn to polypeptides as Group III, are hereby examined.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate

support under 35 U.S.C. 112 for claims 24-28, 30-34, 36-41, 43-48, 50-52 and 54-56, with respect to SEQ ID NO: 764 of this application. Priority date of the instant application is therefore considered to be September 12, 2001. Applicants are requested to provide page and line numbers for support of priority from the numerous applications listed as basis for priority. In addition, if the application from which priority is claimed, please indicate whether there is a computer readable format of the Sequence Listing.

Claim Rejections - 35 USC § 101/112

The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

- Claims 24-57 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by either specific and/or substantial utility or a well-established utility.

The claimed protein of claims 24-57 are not supported by a specific asserted utility because the disclosed uses of these compositions are not specific and are generally applicable to any predicted polypeptide sequence that was derived from computational analyses of the cDNA sequence. (Please note that the physical protein itself is not supported by the specification, all proteins/polypeptides are a mere translation of the nucleic acid sequence):

> [...] the fourth column provides the analysis method by which the homology/identity disclosed in the Table was determined. **Comparisons were made between polypeptides encoded by the polynucleotides of the invention** and either a non-redundant protein database (herein referred to as "NR") or a database of protein families (herein referred to as "PFAM") as further described below. The fifth column provides a description of the PFAM/NR hit having a significant match to a polypeptide of the invention. Column six provides the accession number of the PFAM/NR hit disclosed in the fifth column. Column seven, "Score/Percent Identity", provides a quality score or the percent identity, of the hit disclosed in columns five and six. [...] In specific embodiments polypeptides of the invention comprise, or alternatively consist of, an amino acid sequence encoded by a polynucleotide in SEQ ID NO:X as delineated in columns 8 and 9, or fragments or variants thereof.

The asserted specific utilities are based upon homology/identity to experimentally known sequences after translating the cDNA. It is noted that applicant(s) have listed a sequence which is known in the prior art and which has a high percentage sequence similarity to a claimed sequence. Absent factual evidence, a percentage sequence similarity of less than 100 % is not deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known polypeptide. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed polypeptide and the indicated similar polypeptides of known function and therefore lacks support regarding utility

and/or enablement. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over polypeptides of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Attwood, T [*Science*, vol. 290, no. 5491, pp. 471-473 (2000)]; Gerhold et al. [*BioEssays*, vol. 18, no. 12, pp. 973-981(1996)]; Lopez et al. [*Molecular Biology*, vol. 32, pp. 881-891 (1999)]; Russell et al. [*Journal of Molecular Biology*, vol. 244, pp 332-350 (1994)]; and Wells et al. [*Journal of Leukocyte Biology*, vol. 61, no. 5, pp. 545-550 (1997)].

Further, it is unpredictable if the cDNA that encodes SEQ ID NO: 764 will successfully encode a functional protein in that it is not indicated to be a full-length open reading frame. Since there is no physical protein, the instant invention requires further experimentation to be able to have a protein from which further assays maybe performed to determine and/or validate the actual function of the predicted peptide. The potential specific utility of the protein is determined by sequence characteristic prediction not by experimentation; no actual protein with a defined functionality or biological activity is disclosed thus no certainty to have a useful isolated product with which to perform the potential activity assays suggested in Table 1E for SEQ ID NO: 764. The specification asserts that the polypeptide compounds, proteins, may be useful in a variety functional/biological activities based on a correspondence of similarity to a known protein. Table 1E lists general exemplary activity assays that potentially **may** be useful for SEQ ID NO: 764 (pp. 923-924); assays for assessing the ability of the polypeptide "(including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions" (Table 1E, p.923, 5th column). Ideally, the use of examples in a given specification typically serve to demonstrate at least the critical limitations and/or requirements in order to make/use an invention. However, the examples are generic in nature and not specific to the elected sequence. The elected sequence is identified by the specification by a variety of tables that are based solely on predictive analyses that have no experimental support. The 6th column describes the preferred listing of applications and indications of the polypeptide are non-specific, but covering a wide array of diseases and disorders.

Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.

The above listings include a further laundry list of diseases or disorders that are within the indications themselves for which Hyperproliferative disorders appears to cover an extremely broad range of disorders across the board (specification, pp. 2031-2033) that no specific use has actually been indicated as the preferred embodiment of SEQ ID NO: 764. In fact, the specification summarizes modern biotechnology generally but never connects the elected sequence to any particular or specific utility. This wishlist desire for a utility for the claimed sequence falls short of a readily available utility. The exemplary assays described within the specification are general to any disclosed polypeptide and are non-specific uses that are applicable to proteins in general and not particular or specific to the polypeptide being claimed.

In addition, the protein is not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. For example, the protein is not experimentally characterized in any fashion, but partially characterized by predictions based on homology analyses to public database entries. The research contemplated by applicant(s) to characterize potential protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context or use. Similarly, the other listed and asserted utilities such as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the protein compound(s) such that another non-asserted utility would be well established for the compounds.

- Claims 24-57 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by a specific, substantial, and credible utility, or, alternatively, a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

- Claims 24-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.
  - NEW MATTER: Claims 50-57 are directed to specific fragment peptides that are "at least 30 contiguous amino acid residues" which are not supported by the specification. In addition, the specification lacks support for any specific fragment of SEQ ID NO: 764, or any other sequence. Applicants must point to page and line numbers for amendments to the claims.
  - WRITTEN DESCRIPTION: Claims 24-57 are directed to a predicted polypeptide sequence. Applicants have not experimentally isolated the claimed 'isolated protein', but merely base the description on homology and predictive analyses such as the region of amino acids that may carry characteristics such as signal peptide and secreted peptide.

In addition, the claims are directed to encompass proteins corresponding to sequences of 90% or 95% identity to the overall or portion of SEQ ID NO: 764. The specific 10% or 5% that are not identical to the elected sequence are represented by the claim are not supported by the specification. Although the sequence itself distinguishes the structural features of the nucleic acid, sequences, beyond exact identity (be it in entirety or to contiguous fragments) of the elected SEQ ID NO: 764, are included but not disclosed as to written description. Each variation of the 5% or 10% non-identical, results in a new and independent sequence that does not reliably result in similar or identical biological activities as result for example from altered folding patterns. For example, it would have been known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. As discussed above, in the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Thus the instant claims are directed to encompass peptide sequences that correspond to sequences from other species, mutated fragment sequences, allelic variants, splice variants, and so forth. None of these additional sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

- WRITTEN DESCRIPTION: Claims 30-35, 43-49 and 54-57 are directed to biological deposits. See MPEP 2400:

> The deposit rules (37 CFR 1.801 - 1.809) set forth examining procedures and conditions of deposit which must be satisfied in the event a deposit is required. The rules do not address the substantive issue of whether a deposit is required under any particular set of facts.

Examiner has tried to review the specification for support that demonstrates compliance to the deposit rules, however has been unsuccessful due to the overwhelming length of the specification. Applicant is requested to point to the pages that provided the required information if compliance has been met. If the deposit is not in accordance with the regulations, the claims do not meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the biological deposits of the claims. Please refer to the biological deposit rules 37 CFR 1.801 - 1.809.

Claim Objections

Claims 30-35, 43-49 and 54-57 are objected to due to the claims not further limiting the subject matter of claims 24-29, 36-42 and 50-53 respectively. As disclosed by the specification the polypeptide SEQ ID NO: 764 correlates directly to the HLYEU59 cDNA contained in ATCC Deposit No. 203957, thus it is unclear what are the differences in the metes and bounds of the parameters covered by claim 24 and claim 30 for example. Claim 24 requires the isolated protein to include amino acid residues 25-43 of SEQ ID NO: 764; these residues are indicated in Table 1A (p. 60) to be the 'secreted portion' of the peptide that corresponds to HLYEU59 cDNA: ATCC Deposit No. 203957. Claim 30 requires "the amino acid sequence of the secreted portion of the polypeptide encoded by the HLYEU59 cDNA contained in ATCC Deposit No. 203957"(lines 1-3). Thus the requirements of for example claims 30-35 are the literal translation of the limitations numerically and succinctly described in claims 24-29.

Specification Objections

The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code in the specification in the following place: a) page 17, line 13; b) page 30, line 4; c) page 1906, line 24; and elsewhere in the specification. See MPEP § 608.01.

Conclusion

- Claims 24-57 are rejected under 35 U.S.C. 101/112 – utility.
- Claims 50-57 are rejected under 35 U.S.C. 112, first paragraph – new matter.
- Claims 24-57 are rejected under 35 U.S.C. 112, first paragraph – written description.
- Claims 30-35, 43-49 and 54-57 are rejected under 35 U.S.C. 112, first paragraph – written description, biological deposit.
- Claims 30-35, 43-49 and 54-57 are objected.

No claim is allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (703) 306-0511. The examiner can normally be reached on Monday-Friday from 9 A.M to 5 P.M. If attempts to reach the examiner by telephone are unsuccessful, the primary examiner in charge of the prosecution of this case, Jehanne Souaya, can be reached at 703-308-6565. If attempts to reach the examiners are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Chantae Dessau, whose telephone number is (703) 605-1237, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

July 14, 2003

Monika B. Sheinberg
Art Unit 1634

MBS

JEHANNE SOUAYA
PATENT EXAMINER
Primary

Jehanne Souaya
7/14/03